REMARKS

Claims 144-155, 157-190 and 192-215 are pending. Claims 156 and 191 are canceled. Claims 144, 146-149, 159-160, 169, 172-173, 179-184, 194-195, 201, 204, 207-208 and 214-215 have been amended.

Amended claims 144, 146-147, 179, 181-182 recite the phrase "partial or complete" when referring to a PIV genome or antigenome in order to better define the invention. Support for this phrase is found, *inter alia*, on page 19, at lines 15-18. This text describes that the genome or antigenome of the virus need only contain genes or portions thereof necessary to produce infectious particles, which may be viral or sub-viral (i.e. containing less than all of the viral proteins) particles. Additionally, several embodiments in which a complete viral genome is used are described, e.g. in the description of the Figures 8-10 on page 14, at lines 18-19.

Specific mutations have been deleted in claims 144, 146-147, 172, 173, 179, 181-182 and 207-208 to better define the invention.

The term "molecule" has been deleted from claim 201 to better define the invention.

The phrase "confers a phenotype of attenuation of replication of at least 10 fold in the respiratory tract of a subject infected with a virus" has been deleted from claims 148, 160 and 195 to better define the invention.

The phrase "infectious chimeric PIV being attenuated for replication at least 10 fold in the respiratory tract of a subject infected with a virus" has been deleted in claim 183 to better define the invention.

The term "chimeric" has been deleted from claims 179-182 and claims 214-215 to better define the invention.

The location of a specific mutation has been added to claims 149, 169, 184 and 204. Support for this location is found on page 92 at Table 8.

Claims 144 and 146 have been amended for clarification.

Claim 159 has been amended to change its dependency from canceled claim 156 to claim 154.

Claim 194 has been amended to change its dependency from canceled claim 191 to claim 189.

No new matter has been added by way of these amendments.

Objections to Drawings

The Examiner has objected to the drawings filed on May 28, 1998. Attached herewith are replacement drawings corresponding to Figures 1-19 in the specification as filed.

Rejections under § 102

The Examiner has rejected claims 144-165, 182-200, 214 and 215 under 102(e) as allegedly anticipated by US Patent No. 5,869,036 to Belshe et al. ("Belshe"). Applicants respectfully traverse.

Belshe discloses in only summary fashion nucleic acid constructs encoding from one to three viral proteins (wild-type NP, P and/or L) and cDNA clones of the cp45 genome and hybrids thereof. A schematic drawing of the cp45 genome is provided. From the 3' to 5' direction, the cp45 genome is mutated in every gene but the 5' trailer, (see FIG. 1 of Belshe

relevant to Applicants' arguments regarding cp45), and, therefore, encodes a mutated L gene. When the cp45 virus is transfected into cells at 39.5°C, it has a virus recovery titer of < 1.0. (Table 3). The recovery is increased at 39.5°C when the cp45 virus is co-expressed with one of Belshe's wild-type L protein-encoding nucleic acid constructs. Furthermore, while viruses produced in the experiment of Example 5 may include a wild-type L protein, the genome packaged by these viruses is a cp45 genome, and so includes a mutated L gene.

The Examiner should note that every virus described or suggested by Belshe includes a genome encoding a mutated L protein from cp45. Although the Examiner states on pages 5 and 7 of the office action that "Belshe's construct is a cp45 genome with a wild type L gene introduced" and points to Example 5 to support this contention, it is clear from Example 5 that the cp45 genome does not have the wild-type L gene introduced into it. The wild type L gene is in its own plasmid construct. (See, Exhibit 1, previously filed by Applicants.)

In contrast, independent claim 148 recites a polynucleotide that encodes a chimeric completed partial genome or anti-genome encoding a wild type L protein. The cp45 genome of Belshe, and hybrids thereof, do not encode a wild type L protein. Therefore, claim 148 and claims dependent therefrom are not anticipated by Belshe.

Amended independent claim 144 is drawn to polynucleotides encoding a complete PIV genome that comprises at least one novel sequence selected from SEQ ID Nos. 61, 63, 65, 67, 69, 71 or 73. SEQ ID Nos. 63 and 73 include two mutations in a codon in the F protein-encoding region and L protein-coding region, respectively. Conversely, the corresponding codons in the cp45 genome only contain a single mutation. These novel mutations result in viruses exhibiting reversion resistance superior to those of the prior art. Additionally, SEQ ID Nos. 61, 63, 65 and 67 include the restriction sites *Hpa I*, *Sca I*, *Bam HI* and *Bst XI*, respectively. These restriction sites are not present at the corresponding locations of the cp45 genome. Furthermore, SEQ ID Nos. 69, 71 and 73 do not include the *Eae I*, *Bsr I* and *Ava II* restriction sites. These sites are present, however, at corresponding locations in the cp45 genome. Because

Belshe does not disclose or suggest these specific mutations, claim 144 and claims dependent thereon are not anticipated by Belshe.

Amended independent claim 146, likewise, is drawn to polynucleotides encoding a complete PIV genome that include the three novel sequences, SEQ ID Nos. 69, 71 and 73, described above. Belshe does not disclose or suggest these specific mutations. Therefore, claim 146 and claims dependent thereon are not anticipated by Belshe.

Similarly to claim 148, amended independent claim 183 and independent claim 195 are drawn to a PIV virus comprising a genome that encodes the wild type L protein. As described above, a genome encoding a wild-type L protein is not anticipated by Belshe. Therefore, independent claims 183, 195 and the claims dependent therefrom are not anticipated by Belshe.

The Examiner also has rejected dependent claim 182. Because claim 182 is dependent on independent claim 181,which was not rejected over Belshe, dependent claim 182 contains the novel features included in independent claim 181. Therefore, the rejection of claim 182 is improper and should be withdrawn.

Claim 214 also has been rejected by the Examiner. This claim is drawn to an immunogenic composition comprising the infectious PIV of any one of claims 179-213. Because claims 183 and 195 are allowable over Belshe as explained above, claim 214 should also be allowable over Belshe since it incorporates the novel features of claims 185 or 195. Claim 214 also incorporates the novel features of claim 179, which was not rejected as anticipated by Belshe.

Additionally, claim 215 has been rejected by the Examiner. Claim 215 is drawn to a method for making viruses by expressing isolated polynucleotides according to claims 144-178 in a cell or in a cell-free lysate. Because amended independent claims 144 and 146 and claims

148 and 160 are allowable as explained above, claim 215 also is allowable since it incorporates the novel features of these claims.

For all of the above reasons, Applicants request that the rejection of claims 144-165, 182-200, 214 and 215 as lacking novelty over Belshe be withdrawn.

Rejections under § 103

The Examiner has rejected claims 166-181 and claims 201-215 under USC 103(a) as allegedly obvious over Belshe. Applicants respectfully traverse.

In order to establish a *prima facie* case of obviousness, the combined references must teach or suggest all of the elements of a claim. Independent claim 166 and its dependents, and independent claim 201 and its dependents are drawn to isolated polynucleotides and viruses comprising a PIV genome, respectively, wherein the polynucleotides or genomes encode a heterologous antigenic determinant located between a gene start and a gene end sequence. Although Belshe fails to teach or suggest the insertion of heterologous antigenic determinants between gene start and gene end sequences, the Office Action alleges that insertion of an open reading frame "would only be *appropriate* between a gene start and a gene end sequence." (emphasis added). However, Belshe only discloses that in the "gene sequence which encodes . . . [the desired protein] . . . may be substituted for the corresponding sequence in the cp45 genome." (See Col. 8 lines 59-61). Additionally, Belshe's FIG. 1 does not depict any non-translated, intergenic sequences. Therefore, a person of skill in the art, without the benefit of the instant application, would understand that Belshe teaches substituting, for example, all of the HN gene of the target virus for the corresponding portion in the background genome. Belshe does not suggest, as the Office Action asserts, that "one would be motivated to use the gene start and gene end sequences [of the background genome] in order to retain as much stability as possible when

expressing the heterologous genes." This benefit is recognized only when viewed in conjunction with the instant specification. According to the MPEP at 2142, "impermissible hindsight must be avoided and the legal conclusion must be reached on the basis of the facts gleaned from the prior art." Therefore, independent claims 166 and 201 and claims dependent thereon are non-obvious over Belshe.

Amended independent claim 179 recites novel mutations in the M, F, HN and L protein-encoding regions; and independent claim 181 recites novel mutations in the L protein-encoding region. As explained above, these features are novel and non-obvious over Belshe.

For the above reasons, claims 166-181 and claims 201-215 are non-obvious over Belshe. Applicants request that the rejection be reconsidered and withdrawn.

Rejection for non-statutory double-patenting

The Examiner presents a number of provisional obviousness-type double patenting rejections. Applicants request that these issues should be held in abeyance since prosecution is continuing in both cases and the issue may be resolved by amendments in the various applications. See MPEP 804. If necessary, Applicants will file a Terminal Disclaimer following the procedure outlined in the above-mentioned section of the MPEP.

The present application well-describes and claims patentable subject matter. The favorable action of allowance of the pending claims and passage of the application to issue is respectfully requested.

Should the Examiner contemplate issuance of an Office Action other than a Notice of Allowance, she is respectfully requested to contact Mark J. Nuell (Reg. No. 36,623) at the telephone number of the undersigned below, to conduct an interview in an effort to expedite prosecution in connection with the present application.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17; particularly, extension of time fees.

Dated: MAR 15 2006

Respectfully submitted,

By _____

Mark J. Nuell, Ph.D.
Registration No.: 36,623
BIRCH, STEWART, KOLASCH & BIRCH, LLP
8110 Gatehouse Rd
Suite 100 East
P.O. Box 747
Falls Church, Virginia 22040-0747
(703) 205-8000
Attorney for Applicant

Attachments:
Drawing Replacement Sheets 1-19

AMENDMENTS TO THE DRAWINGS

Please replace the original drawings filed May 22, 1998 with the attached replacement sheets of drawings corresponding to Figures 1-19 in the specification as filed.

The replacement sheets merely improve the line quality the drawings and the image quality of photographic figures and other minor faults of compliance. No new matter is added by the replacement sheets.